UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,190	10/31/2003	Barbara Grimpe	CWR-7779NP	1183

68705 7590 09/19/2008

TAROLLI, SUNDHEIM, COVELL & TUMMINO, LLP
1300 EAST NINTH STREET
SUITE 1700
CLEVELAND, OH 44114

EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
09/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/698,190	GRIMPE ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7,10-17,21-28,35 and 37-54* is/are pending in the application.

4a) Of the above claim(s) *4,7,10,11,14-16,21,22,35 and 37-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,12,13,17 and 23-27* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Advisory Action filed 9/12/2008 has been vacated. Applicant's request for reconsideration of the finality of the rejection of the last Office action (6/3/3008) is persuasive and, therefore, the finality of that action is withdrawn. *The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed on 1 August 2008.*

Claim Status

Claims 1, 4, 7, 10-17, 21-28, 35 and 37-54 are pending. Claims 2-3, 5-6, 8-9, 18-20, 29-34, 36, 55-56 are cancelled. Claims 4, 7, 10-11, 14-16, 21-22, 35, 37-54 were withdrawn by the examiner in the previous Office Action, as being drawn to non-elected inventions. Claims 1, 12-13, 17, and 23-27 are under current examination.

Priority

This application claims benefit from provisional U.S. Application No. 60/423,082 filed 1 November 2002 and claims benefit from provisional U.S. Application No. 60/471,447 filed 16 May 2003. The instant application has been granted the benefit date, 1 November 2002 from the application 60/423,082.

Response to Arguments - Claim Rejections 35 USC § 102

Applicant's arguments (Remarks, pages 11) and Claim amendments, filed 1 August 2008, with respect to claims 29 and 56 have been fully considered and are persuasive. The rejection of claims 29 and 56 under 35 USC 102(b) as anticipated by Margolis et al. (US-5,230,937), has been made moot by the cancellation of claims 29 and 56 on 1 August 2008 and are hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 103

Claims 1, 12-13, 17 and 23-25 rejected under 35 U.S.C. 103(a) as being unpatentable over Moyer (Neurology Today. October 2002; 2(1): 26, 28) in view of Kleesiek (WO01/49831) and further in view of Jen et al. (Stem Cells 2000; 18:307-319) are withdrawn in response to the applicant's arguments.

Applicant's arguments (Remarks, pages 11-13) and Claim amendments, filed 1 August 2008, with respect to claims 1, 12-13, 17 and 23-25 have been fully considered and are persuasive.

The applicant has submitted a 37 CFR 1.131 affidavit which indicates that they invented the subject matter of the instant claims prior to April 11, 2002. This date is prior to the publication of Moyer (Neurology Today. October 2002; 2(1): 26, 28). Because the affidavit was timely filed (1/19/2007), the examiner finds this sufficient to overcome the Moyer reference and therefore, the rejection of claims 1, 12-13, 17 and

23-25 under 35 U.S.C. 103(a) as being unpatentable over Moyer in view of Kleesiek and further in view of Jen et al.

The rejection of claims 1, 12-13, 17 and 23-25 under 35 U.S.C. 103(a) as being unpatentable over Moyer in view of Kleesiek and further in view of Jen et al., has been made moot by the cancellation of claims 29 and 56 on 1 August 2008 and are hereby withdrawn.

Therefore, the examiner hereby withdraws the rejection of claims 1, 12-13, 17 and 23-25 under 35 U.S.C. 103(a) as being unpatentable over Moyer in view of Kleesiek and further in view of Jen et al.

NEW GROUNDS OF REJECTION

Claim Objections

Claim 17 is objected to because of the following informalities: Claim 17 contains a minor grammar error. Claim 17 does not include a comma between "oligonucleotides" and "ribozymes" in line 4 of the instant claim. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 12-13, 17, and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fawcett et al. (Brain Research Bulletin. 1999; 49(6): 377-391) in view of Kleesiek (WO01/49831) and further in view of Jen et al. (Stem Cells 2000; 18:307-319).

Claim 1 is directed to a method of reducing glycosaminoglycan (GAG) content in a glial scar of a mammal comprising administering to the glial scar of the mammal an agent that inhibits the expression and/or activity of a chain initiation enzyme wherein the agent is selected from the group consisting of antisense oligonucleotides, ribozymes, DNA enzymes, and RNAi constructs, the agent targeting a nucleic acid sequence

encoding xylotransferase I (XT-I) or xylotransferase II (XT-II); wherein the agent is administered intrathecally, topically, or locally to the glial scar.

Claim 17 is directed to a method of promoting neuronal regeneration in a subject comprising administering an agent to the to a nervous system lesion to inhibit a GAG chain initiation enzyme, wherein the agent is selected from the group consisting of antisense oligonucleotides, ribozymes, DNA enzymes, and RNAi constructs, the agent targeting a nucleic acid sequence encoding xylotransferase I (XT-I) or xylotransferase II (XT-II); wherein the agent is administered intrathecally, topically, or locally to the nervous system lesion; wherein the neuronal regeneration includes neurite extension into the nervous system lesion.

The remaining claims are directed to the agent being a DNA enzyme (claims 12 and 23) and wherein there is an additional administration of a growth factor or neurotrophic factor (claim 25). Claims 13 and 24 are directed to specific DNA enzymes SEQ ID NO:33 and 39.

Fawcett et al. teach damage to the CNS results in formation of glial scars (abstract) and chondroitin sufphate glycosaminoglycan (GAG) expression is increased around the glial scars of CNS injury (page 382, col.1, lines 1-10) and that GAG expression around glial scars inhibit axon growth (page 382, col.2, lines 8-15). Fawcett et al. teach "disruption of proteoglycan synthesis...has been shown to reduce inhibition [of glial growth]" (page 382, col.2, lines 10-11). Fawcett et al. teach "How might axon regeneration be promoted?...If one wishes to reduce the influence of inhibitory

molecules how might one do it? Essentially the options are to remove the cells that produce them, to reduce their synthesis, to block their activity, or to degrade them."

Fawcett et al. do not specifically suggest using antisense oligonucleotides, ribozymes, DNA enzymes, or RNAi constructs to inhibit XT-I or XT-II.

Kleesiek teaches cloning of cDNA of human and rat xylotransferase-I and xylotransferase-II (XT-I and XT-II) and expression of recombinant proteins (abstract). Kleesiek teaches XT is the initial step enzyme in the biosynthesis of the glycosaminoglycan linkage region. (page 2, lines 8-9). Kleesiek teaches "knowledge of the cDNA sequence of XT allows to use it on gene level such as in gene diagnostic or gene therapy" (page 2, lines 25-26). Kleesiek suggests making medicaments which are inhibitors of xylosyltransferase (page 17, lines 3-4).

Kleesiek does not specifically teach using antisense oligonucleotides, ribozymes, DNA enzymes, or RNAi constructs to inhibit XT-I or XT-II.

Jen et al. is a review article about designing antisense oligonucleotides, ribozymes, and DNAzymes. Jen et al. teaches "the DNAzyme can be made to cleave virtually any RNA that contains a purine-pyrimidine junction" (page 312, col.2). The examiner believes that this teachings along with the teachings of Kleesiek which describe the DNA sequence for xylotransferase-I and xylotransferase-II, make any DNA enzyme obvious.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to reduce GAG content in a glial scar and promote neuronal

regeneration in a subject by inhibiting XT-I or XT-II using antisense oligonucleotides, ribozymes, DNA enzymes, or RNAi constructs.

The person of ordinary skill in the art would have been motivated to combine the teachings of Fawcett et al., Kleesiek, and Jen et al. in a method using DNA enzymes (and other inhibitors of mRNA) to XT-I or XT-II to inhibit glial scar formation and promote neural regeneration. Fawcett et al. suggest that inhibiting synthesis of GAG would promote neuronal regeneration, while Kleesiek et al. suggest inhibiting XT using knowledge of the XT cDNA sequence and Jen et al. suggest ribozyme, DNAzyme and antisense design for any DNA sequence.

Absent evidence to the contrary, an artisan would have expected success, because use of antisense oligonucleotides are well known in the art to inhibit expression of genes by inhibiting mRNA. From the teachings of Kleesiek , it seems possible to use the "knowledge of the cDNA of XT-I and XT-II to make gene therapeutic inhibitors of XT-I and XT-II activity. Finally, Jen et al. suggest that any DNAzyme can be made, using knowledge of a given cDNA. Together, the prior art seems to provide all the known element required for using DNA enzymes for the inhibition of XT-I or XT-II.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (cDNA sequence of XT-I and XT-II; theory of DNAzyme design;

importance of XT in glial scar formation and neuroregeneration) are taught by Fawcett or Kleesiek or Jen. It would be therefore predictably obvious to use a combination of these three elements in a method using DNA enzymes (and other inhibitors of mRNA) to XT-I or XT-II to inhibit glial scar formation and promote neural regeneration. Furthermore, the specific DNA enzymes of SEQ ID NO:33 and 39 would be likewise obvious.

Therefore the method as taught by Fawcett et al. in view of Kleesiek and further in view of Jen et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long
Patent Examiner, Art Unit 1633

/Janet L. Epps-Ford/

Primary Examiner, Art Unit 1633